Q This was sent May 23. What did you do with regard to the statistical report after that?
A Well, I then had a better chance to have a look at the report and over the next month I was able to look at it in detail and make my judgments and conclusions on the report. I then got in contact with Mike Atkinson again to say I was prepared to write a declaration to support the effect of ethanol enhancements.
Q Look at Defendants' Exhibit 35, what appears to be a handwritten note.
(Pause for document examination.)
A I have it.
Q Is that in your handwriting?
A Yes, that's in my handwriting. That is my signature and date at the bottom.
Q The Pete that is addressed there, is that your superior, Dr. Rue?
A That is Dr. Rue, yes.
Q In this brief note you say I have contacted Mike, which is Mr. Atkinson?
A Talked to Michael Atkinson.
Q To say I'm prepared to sign declaration stating that ethanol increases the stability of Zantac Syrup. Had you then completed your review of the statistical report by this time?

A Yes, I had completed the report.
Q With respect to the report what did you conclude about the data that was contained in it?
A I concluded that it did support the enhancing effect of ethanol on the syrup.
Q Was there any portion of the data which you found to be either unreliable or irrelevant?
A Oh, yes. I think if we look at the report itself, I think which is 247 --
Q Right.
A -- I mentioned before that there was some issues with the UK ingredient data, and perhaps if we start with that. The first thing I would like to point out is that this was one program, which was the ethanol-containing syrup, SP88/026, and I noticed that at 45 degrees one of the reported data points was high, and in fact, if you look at Table 1.2 and you look down there, there are a series of programs starting PR2828 and going down to SP88/026, under the 45 degree number the figure of 226.6 is clearly different from the ones above, and to me it looked very much like an outlier. When I read further through the report I realized that Nadeem Elahi looked to see if he could pool the data. That means to combine the data. He carried out a statistical test to see if he could do that and he found he couldn't. That confirmed it was an outlier result at that temperature.

Q In your mind what significance does the finding of an outlier among the UK data mean?

A I think it makes me question the reliability of the data.

Q All of the data?

A Particularly at that particular point, the one at 45 degrees for that program certainly.

Q Was there anything else about the UK data that you found to be less reliable?

A Well, when I then sort of again looked further the 30-degree data, where the data, where the data pooled -- well, let me start again.

Nadeem carried out a statistical test to see if the data at 30 degrees showed a difference between the ethanol and nonethanol studies, and he showed that there was a difference at 30, which was statistically significant and it was in favor of the ethanol programs. The ethanol programs were more stable. Then when you look at the data at 45 it wasn't significant. Okay? So we have on one hand data at 30, which was actually the most important temperature, telling us that there was an effect due to ethanol, but at 45 there was no significant difference between ethanol and no ethanol.

It was that information where the different results, plus the fact there was an outlier route at 45 for

one of the programs that made me believe that the whole data set was unreliable. I was concerned if I went in and picked something in my favor that I could be construed as being, selecting information, so I decided to put all the UK information to one side.

Q If you go to the first page of Plaintiffs' Exhibit 247, the first program numbered one, UK ingredients, you decided to disregard in its entirety?

A I did on the basis of what I just said.

Q Look at the top of the next page with the program caption U.S. ingredients.

A Yes.

Q What was your conclusion with regard to this data?

A Well, here I looked at the data and it was analyzed at 30 degrees and at 45 degrees and these can be seen in Table 2.1, looking at the rate constants for those comparisons. This table tells me that at both 30 degrees and at 45 degrees the syrup containing ethanol has a very significant enhanced stability over the syrup without ethanol. So I concluded from that that was reliable information and could be reported because it was both at 30 and at 45.

Q Look at the next table on the next page, Table 2.3. There is some data there for 30 degrees and 45 degrees that you have just mentioned but also some data for 20 degrees. What was your conclusion with respect to that data?

A Well, this is another feature of the data set. The purpose of comparing ethanol-containing syrups and no-ethanol-containing syrups is to look for difference. If you are going to compare two data sets, then in order to show a difference between them, a difference in stability, then you have to have a fair degree of change. If these things don't change you can't see any difference. If they both stay at 100, they start from 100 and after a few months they are still at 100, you can't see the difference. It's more that over a period of storage there is sufficient change in order for the difference to be seen.

At 30 degrees and at 45 and 37 temperatures there is sufficient degradation occurring to see a difference. The problem with the data at 20 is that even after three years' storage the syrups haven't degraded sufficiently to pick up a difference. To illustrate that point, if you look at the raw data, the data, you can see that the syrups have only degraded 3 percent even after three years, and that is insufficient to show a difference between the syrups containing ethanol and the syrups with no ethanol.

To illustrate my point, we heard this morning about analytical variation. This is one of the things that can affect the validity of a data set.

Analytical variation is something inherent in all measurements. We heard you can actually measure something

that is 10 percent, through variation, these things happen. It's the error in the measurement.

But let's just say for example that the analytical variation is plus or minus 1 percent. If the change in both sets of data, ethanol, no ethanol, is only 3 percent over the test period, then the error is one in three. It's very high.

If, however, you have a bigger change occurring over your storage time, over your test period, say 5 percent, 6 percent, 7, 10 percent, then clearly that error is less, it's one in ten perhaps. That is why it's more reliable.

On this basis, 20 degrees for these particular programs are for all ranitidine syrups, these formulations, it's just too low a temperature, it's inappropriate, there isn't enough change occurring over the period of storage of the test. That means because you can't pick up these differences, that when you project to time points beyond the testing period you build in even more inaccuracies. That is one of the things that happened here in this report. Because as a prediction from that 3 percent, which is as far as the syrups go during the three-year test period, out to what would it be at 5 percent, clearly there is an extra error associated in doing that, there is error in the analysis and error in the projection. All of these things you make a judgments. 20 is too low to look at differences between ethanol and no ethanol. However, at 30 degrees the amount of

degradation occurring is even more. It's at the order of four times. Rather than going off by 3 percent it's going off by 10 percent, something like that.

There is a lot more validity, a lot more confidence in the data being generated because the change is much greater. 30 degrees is the top point of controlled room temperature so it's an appropriate one to use. 20 is too low. On that basis for the U.S. data and also for the UK data I don't think it's relevant.

Q All right. That deals with the second program that is referred to in the introduction to the report. I would like you to move now to the third program, which is titled Definitive Active Experiment, Zantac Syrup, and ask you what conclusions you drew with respect to that data with particular reference to Table 3.2?

A Can I just describe briefly the definitive experiment? These are five programs that were set up and the first one was set up without ethanol, so it's got zero percent ethanol. The other four have got different levels of ethanol in them ranging from 2 and a half percent up to 10 percent. They were all put on stability and then compared after a period of storage. The lowest temperature on there was 37 degrees, also 45 degrees as well.

These results are reported in Table 3.1. The 37 degrees you will see that for no ethanol there is a rate

